

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Factors associated with anxiety and depression among type 2 diabetes outpatients in Malaysia: a descriptive cross-sectional single-centre study.
AUTHORS	Ganasegeran, Kurubaran; Renganathan, Pukunan; Manaf, Rizal; Al-Dubai, Sami

VERSION 1 - REVIEW

REVIEWER	Ivan J Perry Department of Epidemiology & Public Health Western Gateway Building University College Cork
REVIEW RETURNED	18-Feb-2014

GENERAL COMMENTS	<p>This is a generally well written and interesting paper addressing an important practical and scientific issue. However there are significant concerns in relation to the sampling strategy. Specifically, this is a cross-sectional study involving a small and unrepresentative sample of well educated and relatively wealthy patients. The findings are therefore poorly generalisable to the target population of persons with diabetes in Malaysia.</p> <p>The objectives and outcome measures should be specified in terms of both the prevalence and determinants of anxiety and depression in patients with diabetes, (Note the term diabetic is no longer widely used in the literature as many persons with diabetes regard it as inappropriate)</p> <p>The predictors of anxiety and depression would be better explored using multiple logistic as opposed to linear regression.</p> <p>This is a cross-sectional study. The term mixed methods is generally reserved for studies that combine quantitative and qualitative methods.</p> <p>The authors might consider submitting this work as a short preliminary report to a national journal in Malaysia and in future work for an international journal they might consider either a multi-centre clinic based cross-sectional study or ideally a general population survey of the prevalence of anxiety and depression in persons with and without diagnosed diabetes.</p>
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REVIEWER	Kirsty Winkley NIHR Post-doctoral Fellow & Lecturer in Diabetes & Psychology King's College London & Institute of Psychiatry
REVIEW RETURNED	24-Mar-2014

GENERAL COMMENTS	<p>This is an interesting cross sectional study reporting the prevalence and correlates of the symptoms of anxiety and depression in a Malaysian type 2 diabetes outpatient sample. As the authors point out there is sparse literature on Malaysian populations with respect to psychological functioning and diabetes is a significant drain on Asian countries. I would suggest the following minor revisions to the paper:</p> <ol style="list-style-type: none"> 1. Please refer to diabetes not diabetics on p.3, line7, p4, line16 2. it is correct to use the term 'people with diabetes' rather than 'diabetics' (not a noun). See p.3, line7, p.4 line 31. etc. 3.1 Methods, please provide more detail on the hospital and the health system, do people have to pay for medical care/insurance? What happens if no insurance, no treatment? 3.2 Why the age range 13-90 years? Split into young people/adults? 3.3 Household income, please give some examples of equivalent income in US dollars as this will help reader to understand typical Malaysian income levels 3.4 HADS only measures depressive/anxiety symptoms therefore not a diagnostic interview, need to adjust throughout the manuscript 4. Results. probably could cut some of the text as have many tables. Not sure why you used age cut-off of 50 years, present in quartiles? It would be interesting to know more about the youngest age group. Tables, add in cut-offs for depression and anxiety. Headings for table 5 and 6 should be associations not 'predictors' 5. Discussion, limitations section. Why use large age range, problems with this as heterogenous group. Discuss the fact that prevalence of depression and anxiety symptoms, clinical depression and anxiety likely to be much less.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name Ivan J Perry

Institution and Country Department of Epidemiology & Public Health

Room 4.18

Western Gateway Building

University College Cork

Please state any competing interests or state 'None declared': None

Reviewer comments: This is a generally well written and interesting paper addressing an important practical and scientific issue. However there are significant concerns in relation to the sampling strategy. Specifically, this is a cross-sectional study involving a small and unrepresentative sample of well educated and relatively wealthy patients. The findings are therefore poorly generalisable to the target population of persons with diabetes in Malasia.

Author response: Dear reviewer, thank you for your comments. The issue of small sample size and effects on generalisability has already been mentioned in our study limitations.

Reviewer comments: The objectives and outcome measures should be specified in terms of both the prevalence and determinants of anxiety and depression in patients with diabetes, (Note the term diabetic is no longer widely used in the literature as many persons with diabetes regard it as inappropriate)

Author response: Thank you for highlighting these issues. The objectives and outcome measures has been restructured to specify both the prevalence and determinants of anxiety and depression in patients with diabetes. The word "diabetic" has been changed to "diabetes" throughout the manuscript.

Reviewer comments: The predictors of anxiety and depression would be better explored using

multiple logistic as opposed to linear regression.

Author response: Dear reviewer, we used the variables anxiety and depression as continuous variables in our data analysis. Accordingly, we use the linear regression because our dependent variables are continuous variables. It is known that the use of continuous variable in the analysis, gives more power to the results. According to Naggara et al. 2011, the use of data-derived “optimal” cut-points can lead to serious bias and should at least be tested on independent observations to assess their validity. Extreme caution should restrict the application of such results to clinical decision-making. Categorization of continuous data, especially dichotomization, is unnecessary for statistical analysis. Continuous explanatory variables should be left alone in statistical models. Reference is given below:

Naggara O, Raymond J, Guilbert F, Roy D, Weill A, Altman D: Analysis by categorizing or dichotomizing continuous variables is inadvisable: an example from the natural history of unruptured aneurysms. American Journal of Neuroradiology 2011, 32(3):437-440.

Reviewer comments: This is a cross-sectional study. The term mixed methods is generally reserved for studies that combine quantitative and qualitative methods.

Author response: We have deleted descriptions as “mixed methods” study. We have described our study as cross-sectional. To be consistent with Editors requests to provide the full study design, we have described our study design as “descriptive cross-sectional single-centre study”. These changes are reflected in our new study title and the methods part.

Reviewer comments: The authors might consider submitted this work as a short preliminary report to a national journal in Malaysia and in future work for an international journal they might consider either a multi-centre clinic based cross-sectional study or ideally a general population survey of the prevalence of anxiety and depression in persons with and without diagnosed diabetes.

Author response: Dear reviewer, thank you very much for your encouragement and suggestions. We are currently initiating early stage efforts for a multi-center study and we hope to have a successful outcome in the near future.

Reviewer: 2

Reviewer Name Kirsty Winkley

Institution and Country NIHR Post-doctoral Fellow & Lecturer in Diabetes & Psychology

King's College London & Institute of Psychiatry

Please state any competing interests or state 'None declared': None declared

Reviewer comments: This is an interesting cross sectional study reporting the prevalence and correlates of the symptoms of anxiety and depression in a Malaysian type 2 diabetes outpatient sample. As the authors point out there is sparse literature on Malaysian populations with respect to psychological functioning and diabetes is a significant drain on Asian countries. I would suggest the following minor revisions to the paper:

Author response: Dear reviewer, thank you for your suggestions and valuable comments. We have made the relevant changes as requested.

Reviewer comments: Please refer to diabetes not diabetics on p.3, line7, p4, line16

Author response: The word “diabetics” has been changed to “diabetes”. These changes have been made to be consistent throughout the manuscript.

Reviewer comments: It is correct to use the term 'people with diabetes' rather than 'diabetics' (not a noun). See p.3, line7, p.4 line 31. etc.

Author response: Thank you for the suggestions. The word “diabetics” has been changed to “diabetes”. In addition, we have written “people with diabetes” with reference to diabetes in the general population and “patients with diabetes” with reference to our study sample. These changes have been made to be consistent throughout the manuscript.

Reviewer comments: Methods, please provide more detail on the hospital and the health system, do people have to pay for medical care/insurance? What happens if no insurance, no treatment?

Author response: A separate paragraph highlighting these issues has been inserted in the methods part. However if the reviewer suggest to place it in the discussion part, we will do.

Reviewer comments: Why the age range 13-90 years? Split into young people/adults?

Author response: Dear reviewer, firstly the age range was between 18-90 years old and not 13-90 years old as mentioned in the text. This was a typing error and we apologize for the mistake. It has been rectified in the text. Secondly, we tried to explore anxiety and depression in younger age groups, as it will be an interesting finding, through median cut-off points (median was 30), but failed to exhibit any significant findings (a problem that arise usually with categorization of continuous variables) . Given that the large amount of literatures exhibited such findings in older populations, we decided to follow the cut-off points for age as 50 years, and as suggested, it was consistent with the findings exhibited by Khuwaja et al., 2010, being it valid and logical inferences. The reference below was cited in the text:

Khuwaja AK, Lalani S, Dhanani R, Azam IS, Rafique G, White F. Anxiety and depression among outpatients with type 2 diabetes: a multi-centre study of prevalence and associated factors.

Diabetology & Metabolic Syndrome 2010; 2: 72.

Reviewer comments: Household income, please give some examples of equivalent income in US dollars as this will help reader to understand typical Malaysian income levels.

Author response: We have added the equivalent household income in USD dollars in the text and under Table 1.

Reviewer comments: HADS only measures depressive/anxiety symptoms therefore not a diagnostic interview, need to adjust throughout the manuscript.

Author response: We have changed the description in the methods and throughout the manuscript. It is currently described as a tool to measure the level of anxiety and depression instead of a screening/diagnostic tool.

Reviewer comments: Results. Probably could cut some of the text as have many tables. Not sure why you used age cut-off of 50 years, present in quartiles? It would be interesting to know more about the youngest age group. Tables, add in cut-offs for depression and anxiety. Headings for table 5 and 6 should be associations not 'predictors'

Author response: Dear reviewer, given that the large amount of literatures explored psychological distress in older age groups, we initiated efforts during result analyses to possibly explore anxiety and depression in younger age groups through median cut-off point of age. However, our analyses failed to exhibit any significant findings. We decided to proceed with the cut-off points suggested in the study by Khuwaja et al., 2010, owing to logical inferences that older age people were more vulnerable to anxiety and depression due to increased disease complications and social isolation of such age groups. Our results exhibited significant findings. Explanations regarding these findings were included in our discussion part and references were cited. Regarding the tables we used the continuous data, but not the categorized. However, we have mentioned the cut-off points in the methods and we have used it to obtain the prevalence in the results. Regarding results in the text, we have written the results in details because we were following the journal style. However we have tried to follow your suggestions by deleting some of the description in the socio-demographics part from the text. Hopefully, we could satisfy you.

Reviewer comments: Discussion, limitations section. Why use large age range, problems with this as heterogenous group. Discuss the fact that prevalence of depression and anxiety symptoms, clinical depression and anxiety likely to be much less.

Author response: We have made the age cut-offs as 50 years, consistent with previous literatures, as our median cut-offs failed to exhibit significant findings. However, based on your comments, we addressed the large age range and its' effect of heterogeneity as a limitation in the study. In case of any future suggestions for improvement by the reviewer, we will do.